



AF/1652

Docket No.: PF-0576-1 DIV

Response Under 37 C.F.R. 1.116 - Expedited Procedure

Examining Group 1652

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Hillman et al.

Title: EXTRA-CELLULAR ADHESIVE PROTEINS

Serial No.: 09/747,804

Filing Date: December 22, 2000

Examiner: Hutson, R.

Group Art Unit: 1652

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TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Return Receipt Postcard;
2. Brief on Appeal, including Appendix (_ pp., in triplicate); and
3. One (1) Attachment (in triplicate).

The fee has been calculated as shown below.

Claims	Claims After Amendment	Claims Previously Paid For	Present Extra	Other Than Small Entry	Rate	Fee	Additional Fee(s)
Total	7	20	0	x\$18.00		\$	0
Indept.	1	3	0	x\$84.00		\$	0
First Presentation of Multiple Dependent Claims				+280.00		\$	0
Total Fee:						\$	0

X Fee for filing a Brief in support of an Appeal under 37 CFR 1.17(c): \$ 320.00

X Please charge Deposit Account No. 09-0108 in the amount of : \$ 320.00

The Commissioner is hereby authorized to charge any additional fees required under 37 CFR 1.16 and 1.17, or credit overpayment to Deposit Account No. 09-0108. **A duplicate copy of this sheet is enclosed.**

Respectfully submitted,

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Response Under 37 C.F.R. 1.116 - Expedited Procedure
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

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BRIEF ON APPEAL

Sir:

Further to the Notice of Appeal filed April 28, 2003, and received by the USPTO on May 2, 2003, herewith are three copies of Appellants' Brief on Appeal. Authorized fees include the \$ 320.00 fee for the filing of this Brief.

This is an appeal from the decision of the Examiner finally rejecting claims 1 and 13 of the above-identified application.

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(1) REAL PARTY IN INTEREST

The above-identified application is assigned of record to Incyte Pharmaceuticals, Inc. (now Incyte Corporation, formerly known as Incyte Genomics, Inc.) (Reel 012548, Frame 0895), which is the real party in interest herein.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

(3) STATUS OF THE CLAIMS

Claims rejected: Claims 1 and 13
Claims objected to: Claims 2 and 4
Claims allowed: None
Claims canceled: Claims 3-5, 7-12, and 17-34
Claims withdrawn: Claims 6, 15 and 16
Claims on Appeal: Claims 1 and 13 (A copy of the claims on appeal, as amended, can be found in the attached Appendix).

(4) STATUS OF AMENDMENTS AFTER FINAL

There were no amendments submitted after Final Rejection.

(5) SUMMARY OF THE INVENTION

Appellants' invention is directed to an isolated extracellular adhesive protein (EXADH) comprising SEQ ID NO:1 and naturally occurring variants at least 90% identical to SEQ ID NO:1 and having extracellular adhesion activity. The invention also provides composition products and methods of making and using the claimed invention.

(6) ISSUES

1. Whether claims Claims 1 and 13 directed to EXADH polypeptide sequences meet the written description requirement of 35 U.S.C. §112, first paragraph.

(7) GROUPING OF THE CLAIMS

As to Issue 1

All of the claims on appeal are grouped together.

(8) APPELLANTS' ARGUMENTS

Claims 1 and 13 stand rejected under 35 U.S.C. § 112, first paragraph, based on the allegation that the claimed invention lacks an adequate written description of the variant polypeptides. The rejection alleges in particular that:

- the question is not whether one would be able to determine whether a given naturally occurring polypeptide is a variant of SEQ ID NO:1, but rather was the applicant in possession of said naturally occurring polypeptide variants of SEQ ID NO:1, such that applicants have adequately described said naturally occurring variants. (Final Office Action at pp. 3-4.)
- To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. (Final Office Action at p. 5.)
- a single polypeptide comprising SEQ ID NO:1 is fully described in the form of SEQ ID NO:1, wherein the polypeptide has extracellular adhesion activity. Those sequences that are “naturally occurring” are a subset of this genus. The specification does not adequately describe this subset according to its structure so that one of skill in the art would be able to predict naturally occurring sequences...(Final Office Action at pp. 5-6.)

The rejection of claims 1 and 13 is improper as the variant polypeptides are adequately described under the requirements of 35 U.S.C. § 112, first paragraph as well as under the case law that further interprets the statute.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

. . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

. . . Mention of representative compounds encompassed by generic claim language *clearly is not required by Section 112 or any other provision of the statute*. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

. . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, *it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by ‘other appropriate language.’* *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

Attention is also drawn to the Patent and Trademark Office’s own “Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1”, published January 5, 2001, which provide that :

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., *complete or partial structure*, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. *If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.* [footnotes omitted, emphasis added]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

1. The specification provides an adequate written description of the claimed “variants” of SEQ ID NO:1

The subject matter encompassed by claims 1 and 13 is either disclosed by the specification or is conventional or well known to one skilled in the art.

First note that the “variant” language of independent claim 1 recites an isolated polypeptide comprising “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.” SEQ ID NO:1 is specifically disclosed in the application (see, for example, page 12, lines 24-31 and Figures 1A and 1B). Polypeptide variants having at least 90% identity to SEQ ID NO:1 are described, for example, at page 14, lines 8-11. Accordingly, the Specification provides an adequate written description of the recited polypeptide sequences.

One of ordinary skill in the art would recognize polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1. Given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1. The Examiner’s position is based upon the theory that, although “a single polypeptide comprising SEQ ID NO:1 is fully described in the form of SEQ ID NO:1, wherein the polypeptide has extracellular adhesion activity”, the subset of naturally occurring polypeptides is not adequately described “according to its structure so that one of skill in the art would be able to predict naturally occurring sequences...” (Final Office Action at pp. 5-6.) Applicants strongly disagree with this position.

Such a position ignores that the polypeptides recited in claim 1 b) *are* described in terms of their structure. That is, the claimed polypeptides are “***at least 90% identical to the amino acid sequence of SEQ ID NO:1***.” The structure of SEQ ID NO:1 is provided in the specification, for example, at pp. 1-2 of the Sequence Listing and Figures 1A and 1B. Definitions of the phrases “percent identity” or “% identity” as well as methods for determining such identity are provided, for example, at p. 9, lines 6-20. A definition of polypeptide “variants,” the types of amino acid changes and substitutions that may be made while still retaining biological or immunological activity, and computer programs well known in the art which provide guidance in identifying such variants may be

found, for example, on p. 11, line 35 to p. 12, line 7. A detailed description of the chemical and structural features of SEQ ID NO:1 which contribute to the characterization of SEQ ID NO:1 and other related proteins as extracellular adhesive proteins, including a description of which amino acid residues must be conserved to retain carbohydrate binding activity is provided, for example, at p. 12, line 30 to p. 13, line 15. 90% variants of the claimed polypeptides are described, for example, at p. 14, lines 8-11.

Furthermore, claim 1, for example, recites not only that the polypeptide “variants” have extracellular adhesion activity as well as having at least 90% sequence identity to SEQ ID NO:1, but also have “*a naturally occurring amino acid sequence.*” Through the process of natural selection, nature will have determined the appropriate polypeptide sequences. Given the information provided by SEQ ID NO:1 (the amino acid sequence of EXADH-1) and SEQ ID NO:3 (the polynucleotide sequence encoding EXADH-1), one of skill in the art would be able to routinely obtain “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity” as recited in claim 1. For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the specification of the instant application. See, *e.g.*, p. 31, line 26 to p. 32, line 1; and Example VI at p. 40. Thus, one skilled in the art need not make and test vast numbers of polynucleotide sequences that are based on the amino acid sequence of SEQ ID NO:1. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature. Moreover, once a candidate polypeptide is identified, its activity can be tested, *e.g.*, using an assay such as that which is set forth in Example X on p. 42.

When provided with the detailed description as noted above, one of ordinary skill in the art “would have understood the inventor to be in possession of the claimed invention at the time of filing”. That is, one of ordinary skill in the art would recognize polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1. Given any naturally occurring polypeptide sequence having extracellular adhesion activity, it would be routine for one of skill in the art to recognize whether it was a

variant of SEQ ID NO:1 and to determine the % identity to SEQ ID NO:1 of the variant. Accordingly, the specification provides an adequate written description of the recited variants of SEQ ID NO:1.

2. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which “DNA claims” have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

In claims to genetic material, however, a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA,” without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. § 112; *i.e.*, “an mRNA of a vertebrate, which mRNA encodes insulin” in *Lilly*, and “DNA which codes for a human fibroblast interferon-beta polypeptide” in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polypeptides in terms of chemical structure as well as functional characteristics. For example, the language of amended independent claim 1 recites both chemical structure and functional characteristics to define the claimed genus:

1. (Once amended.) An isolated polypeptide selected from the group consisting of:
 - a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and
 - b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure as well as the functional characteristics of SEQ ID NO:1. In the present case, Appellants do not rely *solely* on a description of functional characteristics of the claimed polypeptides. The polypeptides defined by the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry “on whatever is now claimed,” the Examiner failed to provide an appropriate

analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

3. The present claims do not define a genus which is “highly variant”

Furthermore, the claims at issue do not describe a genus which could be characterized as “highly variant.” Available evidence illustrates that, rather than being a large variable genus, the claimed genus is of narrow scope.

In support of this assertion, the Board’s attention is directed to the reference by Brenner et al. (“Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships,” Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078)(Attachment No. 1, of record). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues (Brenner et al., pages 6073 and 6076). Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins (Brenner et al., page 6076).

The present application is directed, *inter alia*, to polypeptides related to human prostate carcinoma tumor antigen-1 (PCTA-1), a member of the galectin class of proteins. In particular, the polypeptides are selected from polypeptides comprising SEQ ID NO:1, and polypeptides comprising naturally occurring amino acid sequences at least 90% identical to SEQ ID NO:1 and having extracellular adhesion activity. In accordance with Brenner et al., naturally occurring molecules may exist which could be characterized as human prostate carcinoma tumor antigen-1 or proteins belonging to the galectin class of proteins and which have as little as 30% identity over at least 150 residues to SEQ ID NO:1. The “variant language” of the present claims recites a polypeptide comprising “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity” (note that

SEQ ID NO:1 has 336 amino acid residues). This variation is far less than that of all potential galectin proteins related to SEQ ID NO:1, i.e., those galectin proteins having as little as 30% identity over at least 150 residues to SEQ ID NO:1.

4. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. § 112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those cases was based on the state of the art at essentially the "dark ages" of recombinant DNA technology.

The present application has a priority date of August 10, 1998. Much has happened in the development of recombinant DNA technology in the 18 or so years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these remarkable advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO:1, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polypeptide variants at the time of filing of this application.

5. The Examiner has attempted to apply a standard for written description different from that which is required by law

The Examiner has alleged that claims 1 and 13 do not comply with the requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph because:

- To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus

sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. (Final Office Action at p. 5.)

Applicants submit that neither the written description requirement of 35 U.S.C. 112, first paragraph nor any case law that interprets the statute has ever set forth such a standard. Furthermore, case law in the area of the written description requirement of 35 U.S.C. 112, first paragraph is clear with regard to the details considered sufficient to describe a claimed genus:

. . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

. . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

The specification sets forth a description of the claimed polypeptide variants using “other appropriate language” as indicated above in connection with the remarks regarding “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.” The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:1 and structural requirements for biological and immunological activity at, for example, pp. 1-2 of the Sequence Listing; Figures 1A and 1B; p. 9, lines 6-20; p. 12, line 30 to p. 13, line 15; and p. 14, lines 8-11. The specification provides a means of identifying naturally occurring functional variants having 90% sequence identity with SEQ ID NO:1 and having extracellular adhesion activity at, for example, p. 11, line 35 to p. 12, line 7; p. 31, line 26 to p. 32, line 1; Example VI at p. 40; and Example X at p. 42.

Applicants therefore submit that the “genus is sufficiently identified in [the instant] application by ‘other appropriate language’” as stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960). Furthermore, Applicants submit that “a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing” as stated in the Patent and Trademark Office’s own “Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1”, published January 5, 2001. Accordingly, claims 1 and 13 meet the statutory requirements for written description under 35 U.S.C. 112, first paragraph.

6. Summary

The Office Action failed to base its written description inquiry “on whatever is now claimed.” Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of both the chemical structure and the functional characteristics of SEQ ID NO:1. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action.

Moreover, the Examiner has applied to the subject application a written description standard that has no basis in the law.

For at least the above reasons it is believed that claims 1 and 13 meet the written description requirement of 35 U.S.C. § 112, first paragraph. It is therefore requested that this rejection be reversed.

(9) CONCLUSION

Due to the urgency of this matter and its economic and public health implications, an expedited review of this appeal is earnestly solicited.

If the USPTO determines that any additional fees are due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**.

This brief is enclosed in triplicate.

Respectfully submitted,

INCYTE CORPORATION

Date: July 1, 2003

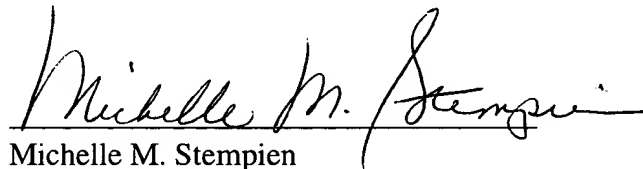


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Attachment (1): Brenner et al., Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078

APPENDIX - CLAIMS ON APPEAL

1. An isolated polypeptide selected from the group consisting of:
 - a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and
 - b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having extracellular adhesion activity.

13. A composition comprising a polypeptide of claim 1 and an excipient.